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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,095	05/03/2001	Jay M. Short	DIVER1280-10	7088

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EXAMINER	
LOEB, BRONWEN	

ART UNIT	PAPER NUMBER
1636	13

DATE MAILED: 11/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/848,095	Applicant(s) SHORT ET AL.	
	Examiner Bronwen M. Loeb	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 Aug 2002, 8 Nov 2002 and 13 Nov. 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *27 August 2002* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Copy of Papers Originally Filed information and Notice to Comply.

DETAILED ACTION

This action is in response to the communications filed 27 August 2002, 8 November 2002 and 13 November 2002. The amendment filed 27 August 2002 amended claims 1, 2, 5, 8, 10, 13, 15, 19, 20, 26-28, 31, 34, 36, 39 and 41 and provided new claims 54 and 55. The communications filed 8 November and 13 November 2002 provided marked up versions of amended claims 39 and 13, respectively.

Claims 1-55 are pending.

Sequence Compliance

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences were set forth that lack sequence identifiers, no computer readable format (CRF) was filed, no paper sequence was filed and no attorney statement was filed. These sequences include **one on p. 25 [0077]**. If the Sequence Listing required for the instant application is identical to that of another application, a letter may be submitted requesting transfer of the previously filed sequence information to the instant application. For a sample letter requesting transfer of sequence information, refer to MPEP § 2422.05. Additionally, it is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP § 2422.02).

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

A reply to a notice to comply with the sequence rules should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office because mail sent to this zip code is destined for irradiation. Computer readable formats, such

as disks and CD's, are destroyed as a result of the irradiation process. The following information is also provided on the website.

Please direct all replies to the United States Patent and Trademark Office via one (1) of the following:

1. Electronically submitted through EFS-Bio (**<http://www.uspto.gov/ebc/efs/downloads/documents.htm>**, EFS Submission User Manual - ePAVE)

2. Mailed to:
U.S. Patent and Trademark Office
Box Sequence, P.O. Box 2327
Arlington, VA 22202

3. Mailed by Federal Express, United Parcel Service or other delivery service to:
U. S. Patent and Trademark Office
2011 South Clark Place
Customer Window, Box Sequence
Crystal Plaza Two, Lobby, Room 1B03
Arlington, Virginia 22202

4. Hand Carried directly to the Customer Window at:
2011 South Clark Place
Crystal Plaza Two, Lobby, Room 1B03, Box Sequence,
Arlington, Virginia 22202

Drawings

2. The corrected or substitute drawings were received on 27 August 2002. These drawings are acceptable.

The drawings are objected to however because the originally filed drawings were provided on 8 ¼ in x 11 ⅝ in paper while the corrected drawings were provided on 8 ½ in x 11 in paper. In accordance with 37 CFR 1.84 (f) all drawings must be on the same-sized paper. Accordingly, Applicant must provide the corrected drawings on 8 ¼ in x 11 ⅝ in, or provide the originally filed drawings on 8 ½ in x 11 in paper.

A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

3. Claim 46 is objected to because of the following informalities: There appears to be a word or phrase missing, such as "library in".

This objection is maintained from the action mailed 20 February 2002. Applicant refers to an amended claim 46 several times in the 27 August 2002 response (pages 7 and 1, and page 6 of Exhibit A) however no clean or marked up version of an amended claim 46 was found.

Appropriate correction is required.

4. While claim 55 is not objected to, the Examiner wonders if Applicant meant to recite that the substrate in claim 54 is a substrate *for* a thioesterase, rather than the substrate itself *is* a thioesterase.

Response to Amendment

5. The terminal disclaimer filed on 27 August 2002 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 6,174,673 has been reviewed and is accepted. The terminal disclaimer has been recorded.

6. The rejection of claims 1-15, 18-41 and 44-53under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,174,673 has been withdrawn in view of Applicant's filing of a terminal disclaimer.

The rejection of claims 16, 17, 42 and 43 are rejected under 35 U.S.C. §101 as claiming the same invention as that of claims 11 and 42 of prior U.S. Patent No. 6,174,673 has been withdrawn in view of Applicant's amendment.

The rejection of claims 26-53 under 35 U.S.C. §112, second paragraph, as being indefinite has been withdrawn in view of Applicant's amendment.

The rejection of claim 28 under 35 U.S.C. §102(e) as being anticipated by Thompson et al (USP 5,824,485) has been withdrawn in view of Applicant's amendment.

The rejection of claim 28 under 35 U.S.C. §103(a) as being unpatentable over Thompson et al in view of Plovins et al (App. Environ. Microbiology (1994) 60:4638-4641) and Zhang et al (FASEB J. (1991) 5:3108-3113) has been withdrawn in view of Applicant's amendment.

The rejection of claim 28 under 35 U.S.C. §103(a) as being unpatentable over Thompson et al in view of Short (USP 6,057,103) has been withdrawn in view of Applicant's amendment.

7. Claims 1-25 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reasons of record and as further discussed below.

Claims 1-4, 6-10, 18, 19, 23-27, 29, 30, 32-36, 39-41, 44, 45 and 51-53, now also applied to claims 16, 17, 42 and 43 as a result of Applicant's amendment, stand rejected under 35 U.S.C. §102(e) as being anticipated by Thompson et al (USP 5,824,485) for reasons of record and as further discussed below.

Claims 1-4, 6-15, 18, 19, 23-27, 29, 30, 32-41, 44, 45 and 51-53, now also applied to claims 16, 17, 42 and 43 as a result of Applicant's amendment, stand rejected under 35 U.S.C. §103(a) as being unpatentable over Thompson et al in view of Plovins et al (App. Environ. Microbiology (1994) 60:4638-4641) and Zhang et al (FASEB J. (1991) 5:3108-3113) for reasons of record and as further discussed below.

Claims 1-10, 18, 19, 20-27, 29, 30-36, 39-41 and 44-53, now also applied to claims 16, 17, 42 and 42 as a result of Applicant's amendment, stand rejected under 35 U.S.C. §103(a) as being unpatentable over Thompson et al in view of Short (USP 6,057,103) for reasons of record and as further discussed below.

8. New rejections, necessitated by Applicant's amendment, are presented below.

Response to Arguments

9. With regard to the rejection of claims 1-25 under 35 U.S.C. §112, second paragraph, as being indefinite, Applicant's arguments have been fully considered but are deemed not persuasive.

Applicant argues that claim 1 has been amended to recite "difference" instead of "change". However amended claim 1 still refers to a "difference" (line 7) in b) and a

"change" (line 10) in c). Thus, the argument is not persuasive and the rejection is maintained.

10. With regard to the rejection of claims 1-4, 6-10, 16-19, 23-27, 29, 30, 32-36, 39-45 and 51-53 under 35 U.S.C. §102(e) as being anticipated by Thompson et al (USP 5,824,485), Applicant's arguments have been fully considered but are deemed not persuasive.

Applicant argues that Thompson et al fails to disclose each and every aspect of the invention and cites two examples. First, it is asserted that Thompson et al does not disclose co-encapsulation in a gel microdroplet of a library clone and a detectable bioactive substrate wherein the bioactive substrate comprises a substrate for the desired biomolecule or bioactivity of interest and a change in the substrate, such as a change in fluorescence, indicates the presence and identity of the bioactivity or biomolecule that can be detected by screening of the microdroplet. Second, it is asserted that Thompson et al fails to disclose insertion into a library clone of a bioactive substrate or of a polynucleotide encoding such a substrate, that the substrate of Thompson is "supplied by the host organism, by other heterologous gene products that are co-expressing in the same host organism, or from the medium" (citing col. 30, lines 2-5) and that the fluorescent probes are non-specific (citing col. 37, lines 10-25). These assertions are not persuasive as Thompson et al explicitly teach co-encapsulation of a library clone and a bioactive substrate (col. 37, lines 37-48 and col. 38, lines 47-65) wherein a signal is generated if the library clone has the desired bioactivity or biomolecule for the bioactive substrate. Thompson et al does not teach only non-

specific fluorescent probes; Thompson et al teaches that an example of a substrate is an enzyme substrate linked to a fluorogenic agent; when the substrate is cleaved by the enzyme, a fluorescent product results (col. 36, line 62-col. 37, line 4). Enzyme substrates are specific to the target enzyme and are thus not non-specific. Screening of the microdroplets is taught including by FACS (col. 39, lines 15-16). The argument that Thompson et al fails to disclose that the substrate is encoded by a polynucleotide is rebutted by the very quote Applicant cites: "substrates...may be provided...by other heterologous gene products that are co-expressing in the same host organism" (col. 30, lines 2-5). It is agreed however that Thompson et al does not teach a polynucleotide encoding an enzyme substrate which has a fluorescence change upon exposure to its enzyme; for this reason, claim 28 has been removed from this rejection under 35 USC §102. However, the other claims remain anticipated and the rejection is maintained.

Claims 16, 17, 42 and 43 have been added as a result of Applicant's amendment. Thompson et al teaches the use of FACS for screening encapsulated clones and substrate (see for instance col. 39, lines 15-16), therefore these claims are anticipated.

11. With regard to the rejection of claims 1-4, 6-15, 16-19, 23-27, 29, 30, 32-45 and 51-53 under 35 U.S.C. §103(a) as being unpatentable over Thompson et al in view of Plovins et al (App. Environ. Microbiology (1994) 60:4638-4641) and Zhang et al (FASEB J. (1991) 5:3108-3113) and the rejection of claims 1-10, 16-19, 20-27, 29-36 and 39-53 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Thompson et al in

view of Short (USP 6,057,103), Applicant's arguments have been fully considered but are deemed not persuasive

Applicant argues that Thompson et al is a deficient reference and that none of the secondary references make up for the alleged deficiencies in Thompson et al. As discussed above, Thompson et al is not a deficient reference in the ways asserted by Applicant. Thompson et al lacked specific teachings as originally set forth in the action mailed 20 February 2002 and the secondary references were cited with respect to these deficiencies and motivation to combine was provided in each instance. One of ordinary skill in the art would have a reasonable expectation of success in each cited combination. Therefore, these rejections are maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claim 28 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is based on the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph "Written Description"

Requirement published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 28 is drawn to a method for identifying bioactivities or biomolecules by detecting a change in the substrate by means of assay or analyzer and wherein the substrate is a polynucleotide encoding an enzymatic substrate. This is a genus claim in terms of any polynucleotide encoding an enzymatic substrate for which a change in the substrate is detectable by an assay or analyzer. The specification mentions fluorescent proteins flanking an enzyme substrate (p. 52 [0182]). This disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all polynucleotides encoding an enzymatic substrate wherein a change in the substrate is detectably by an assay or an analyzer based on the teachings in the specification. A substrate encoded by a polynucleotide will have to be either a nucleic acid or a protein, and would have to have an assay or analyzer-detectable change upon exposure to the enzyme. The specification teaches a substrate flanked by fluorescent proteins and cites WO 97/28261. Since the detectable change is based on fluorescent proteins, the substrate would also have to be a protein. Thus, there is written description for a fusion protein, comprising a protein substrate flanked by fluorescent proteins, which is encoded by a polynucleotide. There is no disclosure of a nucleic acid substrate that is encoded by a polynucleotide and has a detectable change upon exposure to an enzyme. There is no disclosure of any other type of detection other than fluorescence for the bioactive substrate that is encoded by a polynucleotide. Therefore, the specification does not describe the claimed polynucleotides encoding an enzymatic substrate in such full,

clear, concise and exact terms so as to indicate that Applicant has possession of these polynucleotides encoding an enzymatic substrate at the time of filing the present application. Thus, the written description requirement has not been satisfied.

14. Claim 55 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 55 is drawn to the method of claim 54 wherein the substrate is a thioesterase. A fusion protein comprises the substrate, which is flanked by fluorescent proteins. The specification refers to WO 97/28261 with respect to this particular fusion protein. WO 97/28261 (Tsien et al) teaches that the length of the linker between the two fluorescent proteins in these fusion proteins is important with respect to the fluorescent signal generated. While the linker may comprise from 150 to 200 amino acids, only in rare instances will the linker be longer than about 50 amino acids (pp. 20-21 bridging paragraph). A brief search of the literature reveals two thioesterase genes, both of which encode thioesterases which are at least about 300 amino acids in length (Loader et al (1996) and Davies et al (1993)). Based on the teachings in Tsien et al, using an entire thioesterase as the substrate will not work and no detectable change would occur so the claimed method would not operate. Furthermore, the specification does not teach what fragment of any particular thioesterase is to be used as a substrate in the fusion protein or what bioactivity or biomolecule is being screened for using the thioesterase as a substrate. Thus, one of skill in the art would be required to undertake

a large quantity of trial and error experimentation to determine what bioactivity or biomolecule specifically targets thioesterase as a substrate and what fragment of a thioesterase is sufficient to be a substrate while not precluding the fluorescence change associated with the cleavage or change of the fusion protein.

15. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 1-25 and 39-41 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the change" in line 10. There is insufficient antecedent basis for this limitation in the claim.

Claim 13 recites the phrase "wherein samples are heated before step b)" which is vague and indefinite as it is unclear what "samples" are being referred to because claim 1 does not recite any samples.

Claim 39 recites the phrase "wherein samples are heated before step b)" which is vague and indefinite as it is unclear what "samples" are being referred to because claim 27 does not recite any samples.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(e), (f) or (g) prior art under 35 U.S.C. §103(a).

19. Claims 1-4, 6-10, 16-19, 23-30, 32-36, 39-45 and 51-54 are rejected under 35 U.S.C. §103(a) as being unpatentable over Thompson et al in view of Tsien et al (USP 5,981,200). Thompson et al is applied as above and previously to claims 1-4, 6-10, 16-19, 23-27, 29, 30, 32-36, 39-45 and 51-53. Thompson et al does not teach the use of a bioactive substrate that is a polynucleotide encoding an enzymatic substrate (as recited in pending claim 28) or wherein the encoded enzymatic substrate is a fusion of a substrate flanked by fluorescent proteins (as recited in pending claim 54).

Tsien et al teach a fusion protein comprising an amino acid linker which is an enzyme substrate flanked by fluorescent proteins, such as green fluorescent protein. This fusion protein may be encoded by a polynucleotide that can be expressed in recombinant cells in order to screen for enzymatic activity. This advantage of this fusion protein is that enzymatic activity may be screened in vivo and the fluorescent proteins offer greater quantum yield of fluorescence compared to other fluorescent substrates,

such as Edans fluorophore. Furthermore, the fusion protein before and after cleavage are both fluorescent but have distinguishably different characteristics which enables a change in signal rather than loss or gain of a signal. See entire document, especially col. 7, lines 16-37, col. 18, lines 10-47 and col. 21, lines 5-18.

At the time of the invention, it would have been obvious to one of ordinary skill in the art to employ a polynucleotide encoding the fluorescent fusion protein as taught by Tsien et al in the method of Thompson et al. One of ordinary skill in the art would have been motivated to do so, and have expected success, in order to screen for bioactivities in vivo and permit use of FACS screening without needing in vitro generated fluorescent substrates which can be costly both in time and labor needed to make them.

Conclusion

Claims 1-55 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 11:00 AM to 7:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196

Customer service for Tech Center 1600 may be reached at (703) 308-0198.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

November 18, 2002

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Application serial no: 09/848,095

The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

Mailroom Stamp Date	Certificate of Mailing Date
27 Aug 2002	20 Aug 2002 Papers # 7-10

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

COPY OF PAPERS
ORIGINALLY FILED

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

Part of Paper No. 13

Notice to Comply	Application No.	Applicant(s)	
	09/848,095	SHORT ET AL.	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The sequence on p. 25 [0077] lacks a sequence identifier and is not listed in the paper copy or the computer readable form of the Sequence Listing.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

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